

**IN THE CLAIMS:**

Please amend the claims as follows:

3. (Amended) The method according to claim 1, wherein said at least one CTL epitope when presented is associated with an MHC Class I molecule on the surface of the APC and/or wherein said at least one first foreign T<sub>H</sub> epitope when presented is associated with an MHC Class II molecule on the surface of the APC.

4. (Amended) The method according to claim 1, wherein the APC is a dendritic cell or a macrophage.

5. (Amended) The method according to claim 1, wherein the polypeptide antigen is selected from a tumour-associated polypeptide antigen, a self-protein, a viral polypeptide antigen, and a polypeptide antigen derived from an intracellular parasite or bacterium.

6. (Amended) The method according to claim 1, wherein presentation by the APC of the CTL epitope and the first foreign T<sub>H</sub> epitope is effected by presenting the animal's immune system with at least one first analogue of the polypeptide antigen, said first analogue comprising a variation of the amino acid sequence of the polypeptide antigen, said variation containing at least the CTL epitope and the first foreign T<sub>H</sub> epitope.

9. (Amended) The method according to claim 6, wherein substantially all known CTL epitopes of the cell-associated polypeptide antigen are present in the analogue and/or wherein substantially all predicted CTL epitopes of the cell-associated polypeptide antigen are present in the at least first analogue.

10. (Amended) The method according to claim 6, wherein the at least one first analogue further comprises a part consisting of a modification of the structure of the cell-associated polypeptide antigen, said modification having as a result that immunization of the animal with the first analogue induces production of antibodies in the animal against the cell-associated polypeptide antigen.

11. (Amended) The method according to claim 1, which comprises effecting presentation to the animal's immune system of an immunogenically effective amount of at least one second analogue of the polypeptide antigen, said second analogue containing a modification of the structure of the polypeptide antigen, said modification having as a result that immunization of the animal with the second analogue induces production of antibodies against the cell-associated polypeptide antigen.

13. (Amended) The method according to claim 6, wherein the first and/or second analogue(s) comprise(s) a substantial fraction of the cell-associated polypeptide antigen's B-cell epitopes.

14. (Amended) The method according to claim 6, wherein the variation and/or modification involves amino acid substitution and/or deletion and/or insertion and/or addition.

15. (Amended) The method according to claim 6, wherein the variation and/or modification comprises that

- at least one first moiety is included in the first and/or second analogue(s), said first moiety effecting targeting of the analogue to an antigen presenting cell (APC), and/or
- at least one second moiety is included in the first and/or second analogue(s), said second moiety stimulating the immune system, and/or
- at least one third moiety is included in the first and/or second analogue(s), said third moiety optimizing presentation of the analogue to the immune system.

16. (Amended) The method according to claim 6, wherein the variation and/or modification includes duplication of at least one B-cell epitope or of at least one CTL epitope of the cell-associated polypeptide antigen.

17. (Amended) The method according to claim 6, wherein the variation and/or modification includes introduction of a hapten.

18. (Amended) The method according to claim 1, wherein the first and/or second foreign T<sub>H</sub> epitope(s) is/are immunodominant.

19. (Amended) The method according to claim 1, wherein the first and/or second foreign T<sub>H</sub> epitope(s) is/are promiscuous.

20. (Amended) The method according to claim 12, wherein the first and/or second foreign T<sub>H</sub> epitope(s) is/are selected from a natural T<sub>H</sub> epitope and an artificial MHC-II binding peptide sequence.

22. (Amended) The method according to claim 12, wherein the first and/or second T<sub>H</sub> epitopes and/or first and/or second and/or third moieties are present in the form of

- side groups attached covalently or non-covalently to suitable chemical groups in the amino acid sequence of the cell-associated polypeptide antigen or a subsequence thereof, and/or
- fusion partners to the amino acid sequence derived from the cell-associated polypeptide antigen.

24. (Amended) The method according to claim 15, wherein the second moiety is a cytokine selected from interferon  $\gamma$  (IFN- $\gamma$ ), Flt3L, interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 6 (IL-6), interleukin 12 (IL-12), interleukin 13 (IL-13), interleukin 15 (IL-15), and granulocyte-macrophage colony stimulating factor (GM-CSF), or an effective part thereof; a heat-shock protein selected from HSP70, HSP90, HSC70, GRP94, and calreticulin (CRT), or an effective part thereof; or a hormone.

25. (Amended) The method according to claim 15, wherein the third moiety is a lipid such as a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

26. (Amended) The method according to claim 6, wherein the first and/or second analogue(s) has/have substantially the overall tertiary structure of the cell-associated polypeptide antigen.

27. (Amended) The method according to claim 6, wherein presentation by the APC is effected by administering, to the animal, an immunogenically effective amount of the at least one first analogue.

29. (Amended) The method according to claim 27, wherein said at least one first and/or second analogue(s) is/are formulated together with a pharmaceutically and immunologically acceptable carrier and/or vehicle and, optionally an adjuvant.

33. (Amended) The method according to claim 27, which includes administration via a route selected from the oral route and the parenteral route such as the intradermal, the subdermal, the intracutaneous, the subcutaneous; the peritoneal, the buccal, the sublingual, the epidural, the spinal, the anal, and the intracranial routes.

34. (Amended) The method according to claim 27, which includes at least one administration a year, such as at least 2, 3, 4, 5, 6, and 12 administrations a year.

35. (Amended) The method according to claim 1, wherein presentation is effected by administering, to the animal, a non-pathogenic microorganism or virus which is carrying a nucleic acid fragment encoding and expressing the at least one CTL epitope and the at least one  $T_H$  epitope.

36. (Amended) The method according to claim 6, wherein presentation is effected by administering, to the animal, a non-pathogenic microorganism or virus which is carrying at least one nucleic acid fragment which encodes and expresses the at least first analogue.

37. (Amended) The method according to claim 15, wherein the  $T_H$  epitope and/or the first and/or second and/or third moieties are present in the form of fusion partners to the amino acid sequence derived from the cell-associated polypeptide antigen, and wherein presentation is effected by administering, to the animal, a non-pathogenic microorganism or virus which is carrying at least one nucleic acid fragment encoding and expressing the first and/or second analogue.

38. (Amended) The method according to claim 11, wherein presentation is effected by administering, to the animal, a non-pathogenic microorganism or virus which is carrying at least one nucleic acid fragment which encodes and expresses the at least second analogue.

40. (Amended) The method according to claim 1, wherein presentation is effected by in vivo introducing, into the APC, at least one nucleic acid fragment which encodes and expresses the at least one CTL epitope and/or the at least one B-cell epitope, and the at least one first foreign  $T_H$  epitope.

41. (Amended) The method according to claim 6, wherein presentation is effected by in vivo introducing, into the APC, at least one nucleic acid fragment encoding and expressing the first analogue.

42. (Amended) The method according to claim 15, wherein the T<sub>H</sub> epitope and/or the first and/or second and/or third moieties are present in the form of fusion partners to the amino acid sequence derived from the cell-associated polypeptide antigen, and wherein presentation is effected by in vivo introducing, into the APC, at least one nucleic acid fragment encoding and expressing the first and/or second analogue.

43. (Amended) The method according to claim 11, which further comprises in vivo introduction, into the APC, of at least one nucleic acid fragment encoding and expressing the second analogue.

44. (Amended) The method according to claim 1, wherein presentation is effected by in vivo co-introducing, into the APC, at least two nucleic acid fragments, wherein one encodes and expresses the at least one CTL epitope and wherein another encodes and expresses the at least one first foreign T<sub>H</sub> epitope, and wherein the first foreign T<sub>H</sub> epitope is as defined in claim 1.



45. (Amended) The method according to claim 40, wherein the nucleic acid fragment(s) introduced is/are selected from naked DNA, DNA formulated with charged or uncharged lipids, DNA formulated in liposomes, DNA included in a viral vector, DNA formulated with a transfection-facilitating protein or polypeptide, DNA formulated with a targeting protein or polypeptide, DNA formulated with a targeting carbohydrate, DNA formulated with Calcium precipitating agents, DNA coupled to an inert carrier molecule, and DNA formulated with an adjuvant.

46. (Amended) The method according to claim 45, wherein the adjuvant is selected from the group consisting of the adjuvants defined in claim 30.

47. (Amended) The method according to claim 40, wherein the mode of administration is as defined in claim 33.

51. (Amended) A method for the preparation of cell producing an analogue of a cell-associated polypeptide antigen, the method comprising introducing, into a vector, a nucleic acid sequence encoding an analogue which has been selected according to the method of claim 48 and transforming a suitable host cell with the vector.

54. (Amended) The method according to claim 1, wherein the weak cell-associated antigen is selected from the group consisting of 5 alpha reductase,  $\alpha$ -fetoprotein, AM-1, APC, APRIL, BAGE,  $\beta$ -catenin, Bcl2, bcr-abl (b3a2), CA-125, CASP-8 / FLICE, Cathepsins, CD19, CD20, CD21, CD23, CD22, CD33, CD35, CD44, CD45, CD46, CD5, CD52, CD55 (791Tgp72), CD59, CDC27, CDK4, CEA, c-myc, Cox-2, DCC, DcR3, E6 / E7, EGFR, EMBP, Ena78, farsyl transferase, FGF8a or FGF8b, FLK-1/KDR, Folic Acid Receptor, G250, GAGE-Family, gastrin 17, Gastrin-releasing hormone (Bombesin), GD2 / GD3 / GM2, GnRH, GnTV, GP1, gp100 / Pmel 17, gp-100-in4, gp15, gp75 / TRP-1, hCG, Heparanase, Her2 / neu, HMTV, Hsp70, hTERT (telomerase), IGFR1, IL-13R, iNOS, Ki 67, KIAA0205, K-ras, H-ras, N-ras, KSA (CO17-1A), LDLR-FUT, MAGE Family (MAGE-1, MAGE-2, MAGE-3, etc), Mammaglobin, MAP17, Melan-A / MART-1, mesothelin, MIC A/B, MT-MMP's, Mox1, Mucin such as MUC-1, MUC-2, MUC-3, and MUC-4 being abberantly glycosylated, MUM-1, NY-ESO-1, Osteonectin, p15, P170 / MDR1, p53, p97 / melanotransferrin, PAI-1, PDGF, Plasminogen (uPA), PRAME, Probasin, Progenipoietin, PSA, PSM, RAGE-1, Rb, RCAS1, SART-1, SSX gene family, STAT3, STn (mucin assoc.), TAG-72, TGF- $\alpha$ , TGF- $\beta$ , Thymosin  $\beta$  15, TNF- $\alpha$ , TPA, TPI, TRP-2, Tyrosinase, VEGF, ZAG, p16INK4, and Glutathione S-transferase.

57. (Amended) The method according to claim 55 used in the treatment or amelioration of prostate cancer.

60. (Amended) The method according to claim 58 used in the treatment or amelioration of cancer such as prostate cancer and breast cancer.

63. (Amended) The method according to claim 61 used in the treatment or amelioration of breast cancer.

64. (Amended) An analogue of human PSM which is immunogenic in humans, said analogue comprising a substantial part of all known and predicted CTL and B-cell epitopes of PSM and including at least one foreign T<sub>H</sub> epitope as defined in claim 18.

67. (Amended) An analogue of human Her2 which is immunogenic in humans, said analogue comprising a substantial part of all known and predicted CTL and B-cell epitopes of Her2 and including at least one foreign T<sub>H</sub> epitope as defined in claim 18.

70. (Amended) An analogue of human/murine FGF8b which is immunogenic in humans, said analogue comprising a substantial part of all known and predicted CTL and B-cell epitopes of FGF8b and including at least one foreign T<sub>H</sub> epitope as defined in claim 18.

73. (Amended) An immunogenic composition which comprises, as an effective immunogenic agent the analogue according to claim 64 in admixture with a pharmaceutically and immunologically acceptable carrier or vehicle, and optionally an adjuvant.

74. (Amended) A nucleic acid fragment which encodes an analogue according to claim 64.

77. (Amended) The vector according to claim 75 which is selected from the group consisting of a plasmid, a phage, a cosmid, a mini-chromosome, and a virus.

78. (Amended) The vector according to claim 75, comprising, in the 5'63' direction and in operable linkage, a promoter for driving expression of the nucleic acid fragment according to claim 74, optionally a nucleic acid sequence encoding a leader peptide enabling secretion of or integration into the membrane of the polypeptide fragment, the nucleic acid fragment according to claim 74, and optionally a nucleic acid sequence encoding a terminator.

79. (Amended) The vector according to claim 75 which, when introduced into a host cell, is integrated in the host cell genome or is not capable of being integrated in the host cell genome.

80. (Amended) A transformed cell carrying the vector of claim 75.

81. (Amended) A composition for inducing production of antibodies against PSM, Her2 or FGF8b, the composition comprising

- 1) a nucleic acid fragment according to claim 74 or a vector according to claim 75, and
- 2) a pharmaceutically and immunologically acceptable diluent and/or vehicle and/or adjuvant.

82. (Amended) A stable cell line which carries the vector according to claim 75 and which expresses the nucleic acid fragment according to claim 74, and which optionally secretes or carries the analogue according to claim 64 on its surface.

83. (Amended) A method for the preparation of the cell according to claim 80, the method comprising transforming a host cell with the nucleic acid fragment according to claim 74 or with the vector according to claim 75.